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Replacement of a Carboxyl Group by a Halogen

By C. V. WILSON*

In 1861 Borodine (1) reported that dry bromine reacted with silver acetate to give silver bromide, carbon dioxide, and a gas containing bromine which was probably methyl bromide. The subsequent development of this reaction has led to a synthetic method which is a useful tool to the organic chemist (2).

In general, bromide and chlorine react with silver salts of carboxylic acids in inert solvents ($CHCl_3$, CCl_4) to give carbon dioxide, a silver halide, and the halide of a substance containing one less carbon atom than the acid.

$$RCOOAg + X_2 \longrightarrow RX + CO_2 + AgX \quad (A)$$

The reaction is probably somewhat more complex than the equation indicates, for the reaction with iodine has been shown to proceed through an intermediate "iodine triacyl," which gives an iodide in the presence of an excess of iodine (3).

$$3RCOOAg + 2I_2 \longrightarrow 3AgI + I(O{\cdot}COR)_3 \quad (B)$$

$$I(O{\cdot}COR)_3 + I_2 \longrightarrow 3RI + 3CO_2 \quad (C)$$

Excess iodine is essential, for heat alone converts the iodine triacyl to a mixture containing an ester, halide, and acid (or anhydride).

$$I(O{\cdot}COR)_3 \xrightarrow{\text{heat}} CO_2 + RCOOR + RI + RCOOH \text{ (or anhydride)} \quad (D)$$

It will be noted that the method is a valuable supplement to the Hoffmann and Curtius reactions, in which an acid is converted to a primary amine. Frequently the amine is not the product required, but rather the alkyl bromide is prepared from it through the benzoyl derivative. It is much simpler to proceed directly to the alkyl bromide. It is pointed out, however, that the reaction

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(A) has very definite limitations. It has not been applied successfully to the aromatic acids; in most such cases the ring becomes halogenated instead, and the hydrohalide produced removes the silver to give a halogenated aromatic acid.

The method is useful in preparing the following types of compounds:

Alkyl bromides (2)

$$RCOOAg + Br_2 \xrightarrow{CCl_4} R{\cdot}Br + CO_2 + AgBr \quad (E)$$

Alkyl dibromides (2)

$$AgOOC{\cdot}R{\cdot}COOAg + 2Br_2 \longrightarrow Br{\cdot}R{\cdot}Br + 2CO_2 + 2AgBr \quad (F)$$

$$R{\cdot}CHBrCOOAg + Br_2 \longrightarrow R{\cdot}CHBr_2 + CO_2 + AgBr \quad (G)$$

ω-Bromoesters (2)

$$ROOC{\cdot}R'{\cdot}COOAg + Br_2 \longrightarrow ROOC{\cdot}R'{\cdot}Br + CO_2 + AgBr \quad (H)$$

Acyl bromides (2)

$$R{\cdot}CO{\cdot}COOAg + Br_2 \longrightarrow R{\cdot}COBr + CO_2 + AgBr \quad (I)$$

Isocyclic bromides (4)

$$R{>}CHCOOAg + Br_2 \longrightarrow R{>}CHBr + CO_2 + AgBr \quad (J)$$

Aldehyde hydrobromides

$$R{\cdot}CHOH{\cdot}COOAg + Br_2 \longrightarrow R{\cdot}CHOH{\cdot}Br + CO_2 + AgBr \quad (K)$$

In these reactions the bromine can be replaced successfully by dry chlorine. Recent work (3) indicates that an excess of iodine will give iodides, though earlier work in which iodine was not used in excess led to esters (5). An excess of bromine and chlorine also improves the yields of the corresponding halides. Mercury, thallium, and potassium salts can be used but the yields are usually lower and the reactions more sluggish. Mercury salts give the best yields with carbon disulfide as the solvent, while carbon tetrachloride is preferred for other salts.

The reaction has recently found application in the synthesis of long chain ω-bromoesters which are useful materials in the synthesis of musks, in the synthesis of cantharidine and adamantane, and in degradation studies on sterols.

References

(1) Borodine, *Ann.*, *119*, 121 (1861).

(2) Hunsdiecker and Hunsdiecker, *Ber.*, 75, 291 (1942); Luttringhaus and Schade, *Ber.*, 74, 1565 (1941).

(3) Oldham and Ubbelohde, *J. Chem. Soc.*, *1941*, 368.

(4) Hunsdiecker *et al.*, German Patent 730,410.

(5) Simonini, *Monatsh.*, *14*, 81 (1893); Demjanow and Dojarenko, *Ber.*, *40*, 2594 (1907).

New Syntheses of Intermediates in the German Chemical Industry

By R. LEONARD HASCHE*

The first part of this article appeared in the previous issue (Vol. 20, No. 4, 1948).

During the latter part of the war a large plant was put into operation at Ludwigshafen to produce butadiene from acetylene and formaldehyde by a process developed by Reppe. The process was carried out in four steps as follows:

$$2CH_2O + C_2H_2 \rightarrow HOCH_2C{\equiv}CCH_2OH \rightarrow$$

$$HOCH_2CH_2CH_2CH_2OH \rightarrow \begin{array}{c} CH_2{-}CH_2 \\ | \quad\quad \diagdown O \\ CH_2{-}CH_2 \end{array} \rightarrow$$

$$CH_2{=}CHCH{=}CH_2.$$

The first step, called the "alkynol" reaction, is carried out with a catalyst consisting of copper acetylide on silica gel. Acetylene is passed into a formaldehyde solution containing the catalyst at 100°C and 5 atmospheres pressure. Propargyl alcohol is formed as a by-product by the reaction of one molecule of formaldehyde and one of acetylene. The 2-butyne-1,4-diol is then hydrogenated by passing it through a tower of copper-nickel catalyst in the presence of hydrogen at 80°-100°C and 200-300 atmospheres to produce 1,4-butanediol in a

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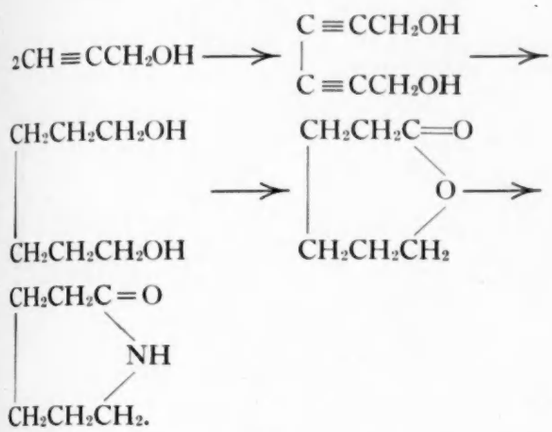
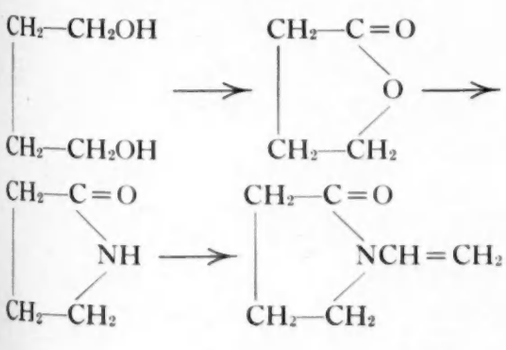
96 per cent yield. On heating the dilute aqueous solution with a small amount of phosphoric acid at 300°C and 100 atmospheres, the butanediol quantitatively forms tetrahydrofuran. In the last step of the process tetrahydrofuran and water vapor are passed over a phosphate catalyst at 200°-260°C to produce butadiene.

Although the process is multistage, the overall yield is excellent. The intermediate products open many avenues for syntheses of new products; for example, caprolactam can be produced from propargyl alcohol as follows:



Caprolactam can be polymerized to a polyamide of the nylon type. Likewise tetrahydrofuran is a valuable intermediate; for example, it can be reacted with two molecules of carbon dioxide and one molecule of water at 270°C and 200 atmospheres with a nickel carbonyl catalyst to give a 90 per cent yield of adipic acid.

The 1,4-butanediol is dehydrogenated in a tower using a copper catalyst at 200°C to form γ-butyrolactone; the latter with ammonia gives pyrrolidone, which on treatment with acetylene yields N-vinylpyrrolidone.



The polymerized N-vinylpyrrolidone in a water solution is used extensively as a blood substitute called "periston."

I. G. Farben prepared many other new intermediates by reacting acetylene with related compounds, such as higher aldehydes, ketones, amines, alkylol amines, mercaptans, and thiophenols. However, the basic reactions were those indicated, namely—"vinylation," "carbonylation," and "alkynolation."

Oxo Synthesis

The so-called "Oxo" synthesis was another important development made by the Germans during the last few years of World War II. It was put into operation at the Ruhrchemie plant in the Ruhr Valley and at the synthetic petroleum plant at Leuna as a joint venture by Ruhrchemie, I. G. Farben, and Henkel.

The "oxonation" reaction has a wide application to compounds having a double bond and to cyclic ethers. However, in the case of conjugated systems, reaction occurs with only one of the double bonds. [The chemistry of this process was discussed in "The Oxo Process" by C. F. H. Allen, *Synthetic Organic Chemicals*, *18*, 3 (1946).]

Cyclopolyolefins

One of the latest reactions studied by Reppe was acetylene polymerization to form a cyclopolyolefin which proved to be cyclooctatetraene.

Acetylene was reacted at 60°-70°C and 15-20 atmospheres with a nickel cyanide catalyst dissolved in tetrahydrofuran. The compound is a golden-yellowish liquid of boiling point 142°-143°C. The chemistry of cyclooctatetraene has been widely discussed in many recent papers and need not be repeated here.

None of the statements made in this article should be considered as recommendations for the use of this information in violation of any patents now in force, or which may be issued in the future. It is assumed that anyone making use of any of the information contained herein will make the usual patent investigations.

New Eastman Organic Chemicals

P 6101 Acetoacet-o-anisidine (Pract.) MP 83-85° ..... 500 g. .. $4.00 D
$CH_3COCH_2CONHC_6H_4OCH_3$ . . . MW 207.22

P 5903 Aminohydroquinone Diethyl Ether (Pract.)
MP 84-86° ..... 1 kg... 5.50 E
2-$NH_2C_6H_3$-1,4-$(OC_2H_5)_2$ . . . MW 213.23

P 5999 Aminohydroquinone Dimethyl Ether (Pract.)
MP 81-83° ..... 1 kg... 5.50 E
2-$NH_2C_6H_3$-1,4-$(OCH_3)_2$ . . . MW 153.18

P 5995 Bromotrichloromethane (Pract.)
MP –7.5° to –7° ..... 1 kg... 4.80 E
$BrCCl_3$ . . . MW 198.30

2693 n-Butyl Itaconate BP 146-148°/11 mm. ..... 1 kg... 3.70 E
$CH_3(CH_2)_3OCOC(:CH_2)CH_2COO(CH_2)_3CH_3$ . . . MW 242.31

P 5959 2,8-Diaminoacridine Sulfate (Pract.) ..... 100 g. .. 4.00 C
$H_2NC_6H_3CH:C_6H_3(NH_2):N\cdot H_2SO_4$ . . . MW 307.32

5996 Dibromochloromethane BP 25-27°/16 mm. ..... 500 g. .. 5.50 D
Br_2CHCl . . . MW 206.87

P 5998 1,2-Dibromo-1,1-dichloroethane (Pract.)
BP 59-60°/11 mm. ..... 500 g. .. 4.25 D
$BrCCl_2CH_2Br$ . . . MW 255.34

5997 Dibromodichloromethane MP 21-22° ..... 500 g. .. 6.50 D
Br_2CCl_2 . . . MW 242.76

T 5278 x,x-Dichlorophthalic Anhydride (Techn.) ..... 500 g. .. 4.80 D
$Cl_2C_6H_2(CO)_2O$ . . . MW 217.01

P 6102 *trans*-2,5-Dimethylpiperazine (Pract.)
MP 114-116° ..... 500 g. .. 7.00 D
$NHCH(CH_3)CH_2NHCH(CH_3)CH_2$ . . . MW 114.19

2692 Ethyl Itaconate BP 104-106°/12 mm. ..... 1 kg... 3.60 E
$C_2H_5OCOC(:CH_2)CH_2COOC_2H_5$ . . . MW 186.20

P 5251 n-Hexylamine (Pract.) BP 128-131° ..... 1 kg... 3.40 E
$CH_3(CH_2)_5NH_2$ . . . MW 101.19

5988 Imidazole-4,5-dicarboxylic Acid MP 296° dec. ... 10 g. .. 2.00 B
$NHCH:NCHCOOHCHCOOH$ . . . MW 158.07

P 5986 2-Methoxyethyl Vinyl Ether (Pract.)
BP 106-108° ..... 1 kg... 5.00 E
$CH_3OCH_2CH_2OCH:CH_2$ . . . MW 102.03

5992 *dl*-Tyrosine MP 305° dec. ..... 100 g. .. 5.50 C
4-$HOC_6H_5CH_2CHNH_2COOH$ . . . MW 181.19